Amendments to the Specification

Please replace paragraph 37 of the specification as filed with the following paragraph:

[37] Figure 28 ~~Figures 28-33~~ depicts an example ~~examples~~ of the interpolating empirical probability function for various values.

Before paragraph 38, please insert the following paragraphs:

[38] Figure 29 depicts an example of the interpolating empirical probability function for various values.

[39] Figure 30 depicts an example of the interpolating empirical probability function for various values.

[40] Figure 31 depicts an example of the interpolating empirical probability function for various values.

[41] Figure 32 depicts an example of the interpolating empirical probability function for various values.

[42] Figure 33 depicts an example of the interpolating empirical probability function for various values.

Please replace previously labeled paragraph 57 (which will be paragraph 62 with the above insertion) with the following paragraph:

[57] Figure 5 is a schematic block diagram depicting the hardware interface processor 205 associated with the bedside device 107. Hardware interface processor 205 comprises a micro controller 503 that communicates via a tri-state bus interface 501 to control blanking circuitry 301, sense electronics module 201, and stimulation electronics module 203. It also notifies signal processor 207 when data is available for further processing.

Please replace previous paragraph 61 (now paragraph 66 with the insertion) with the following paragraph:

[61] Figure 8 shows a functional diagram of an example of a seizure detection algorithm 800 that may be used. Generally, the seizure detection algorithm 800 is capable of detecting brain activity changes based on the spectral characteristics, intensity (ratio), spread, and duration of an electrical (EEG, ECoG, and/or EKG) signal 801 that is obtained from a set of electrodes. In the embodiment of external system 100, eight ECoG channels may be supported, although other embodiments may support a different number of channels. The analog EEG or ECoG data from the electrodes 101 are transformed to digital data with an A to D converter in the bedside device 107. In the hybrid system 1000, the A to D converter may be in the implantable device 953. A digital filter such as a finite impulse response (FIR) filter 803 is configured to estimate the power spectrum density characteristics of a set of electrical brain signals. A foreground determinator 805 associates a foreground value of the signals with a moving foreground interval of a predetermined time length (e.g., 2-seconds), which may be programmable. In the embodiment, foreground determinator 805 squares the value of each sample in the foreground interval and selects the median value. A background determinator 807 associates a background value with a moving background interval of predetermined time length (e.g., 30 minutes), which again may be programmable. At any point in time, the current foreground and background values are computed, respectively, from the foreground and background intervals that immediately precede that time point. Background determinator 807 squares the value of each sample in the background interval and selects the median value. The seizure detection algorithm 800 then processes the results of background determinator 807 through an "exponential forgetting" adjustor 809 that combines the results with previous results from background determinator 807 to produce a an exponentially-smoothed background value. A module 811 then divides the foreground value by the exponentially-smoothed background value to determine a ratio for each signal from each electrode in a selected electrode group. Module 811 also determines the largest ratio from the group of electrodes. The value of the largest ratio is then fed into a detection criterion module 813, which analyzes the sequence of largest ratios to determine when an event is detected. Output 814 from algorithm 800 includes notification that an event has occurred

("detection") as well as variables quantifying the event (e.g., ratio, extent of spread, and duration from all electrodes).

Please replace previous paragraph 66 (now paragraph 71 with the insertion) with the following paragraph:

[66] An apparatus 1000 (e.g., the external device 950) is powered by a rechargeable/replaceable battery 1025 and is voltage regulated by a voltage regulation circuit 1019. A DSP controller 1005 processes neurological data from implantable device 953 and records/stores processed data in a boot flash memory 1007 or in a compact flash memory 1023, which extends the recording capability of memory 1007. The apparatus 1000 may be instructed by a user through buttons 1013. The corresponding inputted information is received by a peripheral interface control (PIC) microprocessor 1011 through a RS232 interface 1017. The user may instruct the DSP controller 1005 to process, store, and retrieve neurological data through PIC microprocessor 1011. The DSP controller 1005 is coupled to a memory 1009 and a speaker 1027. Also, the user may obtain information (e.g., status and selected processed data) through an LCD screen 1015.

Please replace previous paragraph 67 (now paragraph 72 with the insertion) with the following paragraph:

[67] Figure 11 is a schematic block diagram of the implantable device 953 for the hybrid control system of Figure 9. An apparatus 1100 (e.g., the implantable device 953) is implanted in conjunction with a set of electrodes 1101. (In the exemplary embodiment shown in Figure 11, the set of electrodes 1101 comprises eight electrodes.) A reference electrode 1103 is another electrode that is not included in the set of electrodes 1101 and that is not typically involved with the neurological activity as the set of electrodes 1101. The apparatus 1100 communicates with the external device 1000 through a telemetry transceiver 1127 that is coupled to control registers 1109, an antenna 1125, and a telemetry link ~~1023~~ 1123. The apparatus 1000 (e.g., the external device 950) may collect data from the apparatus 1100 by placing a patch antenna 955 on the

patient's body over the implantable device 953 to thereby communicate with antenna 1125 of the apparatus 1100.

Please replace previous paragraph 68 (now paragraph 73 with the insertion) with the following paragraph:

[68] Each electrode of the set of electrodes 1101 may either receive a neurological signal or may stimulate surrounding tissue. Stimulation of any of the electrodes contained in the electrode set 1101 is generated by a stimulation IC 1105, as instructed by a microprocessor 1119. When stimulation is generated through an electrode, the electrode is blanked by a blanking circuit 1107 so that a neurological signal is not received by channel electronics (e.g., amplifier 1111). When microcontroller 1119, which is coupled to 1 MHz crystal oscillator 1121, determines that a channel shall be able to receive a neurological signal, an analog to digital converter (ADC) 1113 samples the neurological signal at a desired rate (e.g., 250 times per second). The digitized neurological signal may be stored in a waveform memory 1115, which is coupled to the microcontroller 1119 via AD bus 1117, so that the neurological data may be retrieved by the apparatus 1000 when instructed.

Please replace previous paragraph 69 (now paragraph 74 with the insertion) with the following paragraph:

[69] **IMPLANTED SYSTEM** – Figure 12 shows an embodiment of an implanted system 10 for treatment of a nervous system disorder in accordance with another embodiment of the invention. As discussed, although the implanted system 10 is discussed in the context of providing brain stimulation, it will be appreciated that the implanted system 10 may also be used to provide other treatment therapies at the brain or head or at other locations of the body. The implanted system 10 generally includes an implanted device 20 coupled to one or more therapy delivery elements 30. The therapy delivery elements 30, of course, may also serve as monitoring elements to receive a neurological signal. The implanted device 20 may continuously or intermittently communicate with an external programmer 23 (e.g., patient or physician programmer) via telemetry using, for example, radio-frequency signals. In this embodiment,

each of the features and functionalities discussed herein are provided by the implanted device 20. As depicted, the external programmer 23 is coupled to a coil antenna 24 via wire 24a.

Please replace previous paragraph 71 (now paragraph 76 with the insertion) with the following paragraph:

[71] As an example to illustrate other embodiments of treatment therapies, Figure 13 shows a medical device system 110 that may be implanted below ~~the~~ a skin 125 of a patient for delivery of drug to a patient as the form of treatment therapy. Device 10 has a port 14 into which a needle can be inserted through the skin to inject a quantity of a liquid agent, such as a medication or drug. The liquid agent is delivered from device 10 through a catheter port 20 into a catheter 22. Catheter 22 is positioned to deliver the agent to specific infusion sites in a brain (B) through bone 123 via distal end 115 of tube 22a, although any location in the body may be utilized. As depicted, sensor 130 may include individual electrodes 26, 28 and 30 positioned on a tube. As it relates to the delivery of drug, device 10 may take a form of the like-numbered device shown in U.S. Patent No. 4,692,147 (Duggan), assigned to Medtronic, Inc., Minneapolis, Minnesota and is incorporated herein in its entirety. The device 10 may be augmented to provide the various functionalities of the present invention described herein.

Please replace previous paragraph 74 (now paragraph 79 with the insertion) with the following paragraph:

[74] Figure 14 discloses one embodiment of such a relaying module in the form of a device that is worn, for example, on the patient's wrist. In such an arrangement, the implanted component 1405 of the medical device system communicates with the relaying module 1415 via telemetry antenna 1410. Similarly, the external component, which includes an external wearable signal processor 1425 that is coupled to audio output 1430 and is in communication with physician programmer 1435, communicates with the relaying module 1415 via antenna 1420. In the embodiment, a telemetry link 1421 between relaying module 1415 and antenna 1420 comprises a 3 MHz body wave telemetry link. To avoid interference, the relaying module 1415 may communicate with the external and implanted components using differing communication

schemes. In some embodiments, the reverse direction and the forward direction of telemetry link 1421 may be associated with different frequency spectra. The relaying module 1415 thereby provides a greater range of communications between components of medical device system. For example, in the embodiment of the implanted system 10, the external programmer 23 may communicate with the implanted device 20 from a more remote location. The external programmer 23 may be across the room and still be in communication via the relaying module 1415. Similarly, in the embodiment of the hybrid system 1000, the external device 950 may be located further away than being worn by the patient. With the telemetry booster stage, the use of hybrid system 1000 is more convenient to the patient in particular at night while sleeping or when taking a shower, eliminating the need for the external device 950 to be worn on the body.

Please replace previous paragraph 77 (now paragraph 82 with the insertion) with the following paragraph:

[77] Figure 15 shows a top-level flow diagram for a clock synchronization and calibration process 1500. For clarity, the following discussion is provided in the context of the external system 100, although other embodiments are possible. ~~In~~ The process starts at step 1501 and in step 1503, a user initiates a study and sets-up the parameters through programmer 109 in step 1505. In the embodiment, the user enters a selected time (through programmer 109) that is different (which may be greater) than the reference time that is associated with monitoring equipment 105. (The reference time may comprise the associated date such month and day.) When the user determines that the time associated with monitoring equipment 105 equals the selected time, the user synchronizes the clocks in step 1507. Consequently, programmer 109 may generate a control message to bedside device 107 to synchronize the clock of bedside device 107. In the embodiment, the user selects an icon; however, other embodiments may use a Global Positioning System (GPS) clock reference or use a control line from monitoring equipment to activate the synchronization of clocks. In step 1509, programmer 109 determines if the clocks of bedside device 107 and programmer 109 were successfully synchronized and notifies the user through a real-time data display of programmer 109. In step 1511, the external system 100 starts run mode operation in which the medical device system may operate its intended functions.

Please replace previous paragraph 78 (now paragraph 83 with the insertion) with the following paragraph:

[78] During the operation of the external system 100 over time, the clocks of monitoring equipment 105, programmer 109, and bedside device 107 may drift with respect to each other. In the embodiment, the clocks of programmer 109 and bedside device 107 are calibrated using the clock of monitoring equipment 105 as a reference. In step 1513, the programmer 109 notifies the user that calibration should be performed (e.g., every 12 hours, although other time periods may be utilized). The user consequently enters a selected time (through programmer 109) that is greater than the present time that is associated with monitoring equipment 105. When the user determines that the time associated with monitoring equipment 105 equals the selected time, the user calibrates the clocks in step 1513. With the calibration process, the clocks of bedside device 107 and programmer 109 are not modified. Rather a "drift" time (equal to the difference between the clock in bedside device 107 and monitoring equipment 105) is stored to a file. Data that are subsequently collected by bedside device 107 can be correlated to the time of monitoring equipment 105 by adjusting the time of bedside device 107 by the drift time. (In the embodiment, the drift time is determined by the difference between the current time of the second clock and the reference time of the first clock.) However, if the drift time is determined to be greater than a predetermined threshold (e.g., one second) in step 1515, programmer 109 may notify the user that the clocks need to be re-synchronized or more frequently calibrated to accurately track the drift between the clocks. If that is the case, the clocks are synchronized in step 1517. In step 1519, the operation is continued.

Please replace previous paragraph 79 (now paragraph 84 with the insertion) with the following paragraph:

[79] Figure 16 shows specific flow diagrams for clock synchronization and calibration in relation to Figure 15. Steps ~~1601-1609~~ 1601, 1603, 1605, 1607 and 1609 correspond to synchronizing the clocks in the external system 100 as shown in steps 1507 and 1517. Steps ~~1611-1619~~ 1611, 1613, 1615, 1617 and 1619 correspond to manually calibrating the clocks as

shown in step 1513. Additionally, as shown in steps ~~1621-1629~~ 1621, 1623, 1625, 1627 and 1629, the external system 100 may periodically (e.g., every 10 minutes) calibrate the clocks of the programmer 109 and bedside device 107 without requiring intervention by the user. In step 1623, programmer 109 retrieves the time from bedside device 107. Programmer 109 compares its time with the retrieved time from bedside device 107 and calculates an updated drift time. Programmer 109 stores the adjusted drift time for correlating times subsequently. As discussed, synchronization may also be utilized in either the hybrid or implanted systems. For example, in the embodiment of the implanted system, the implanted device may provide to or receive from an external component (e.g., patient or physician programmer, video equipment, testing equipment) a clock synchronization/calibration signal, and the calibration/synchronization techniques discussed herein may be utilized to correspond the implanted device with the one or more external devices. Moreover, the clock reference (i.e., the reference clock to which all other clocks would be synchronized/calibrated) may be the clock in the implanted component, one of the external components, a GPS clock, an atomic clock, or any other reference clock.

Please replace previous paragraph 101 (now paragraph 106 with the insertion) with the following paragraph:

[101] A time event 1907 corresponds to a clinical behavior onset time (CBOT), in which a patient manifests the symptoms of the neurological event (such as demonstrating the physical characteristics of a seizure). (In some cases, the patient may not manifest the symptoms even though an ITEO occurs.) Typically, if monitoring elements (such as electrodes) are appropriately positioned, the CBOT will occur after the ITEO. However, if the electrodes are placed away from a point of the neurological event, the CBOT may occur before the ITEO because of a delay of the neurological signals propagating through different portions of the patient's brain. A time event 1909 corresponds to an investigator seizure electrographic termination time, in which the electrographic activity sufficiently decreases. As depicted, clinical seizure duration 1911 extends between the CBOT 1907 and ISETT 1909.

Please replace previous paragraph 102 (now paragraph 107 with the insertion) with the following paragraph:

[102] To illustrate an embodiment of a screening procedure for a particular nervous system disorder, Figures 20 and 21 show flow diagrams for a seizure screening process to define treatment therapy according to an embodiment of the invention. Process 2000 comprises a baseline algorithm monitoring sub-process 2003 (comprising steps 2005-2049) and a trial screening sub-process 2151 (comprising steps 2153-2179). As depicted, the process 2000 starts at step 2001 and in ~~In~~ step 2002, a physician implants electrodes into a patient in order to conduct process 2000.

Please replace previous paragraph 105 (now paragraph 110 with the insertion) with the following paragraph:

[105] In step 2027, which comprises sub-steps 2029 and 2031, the correctness of electrode placement for seizure detection is verified. In sub-step 2029, the ITEO (investigator time of electrographic onset corresponding to time event 1903 in Figure 19) and the CBOT (clinical behavior onset time corresponding to time event 1907 in Figure 19) are provided to the medical device system. (In the embodiment, step 2027 is optional so that the clinician need not provide ITEO and CBOT to the medical device system.) In sub-step 2031, the medical device system determines if the ITEO did not occur after the CBOT. In the embodiment, the fact that the CBOT occurs before the ITEO is indicative that the selected electrodes are not sufficiently near the focus. In such a case, ~~step 2032 determines whether~~ it can be determined to stop screening. ~~If so, screening is ended in step 2034.~~ that the process may end. Otherwise, step ~~2004~~ 2002 allows the physician to reposition subdural and/or DBS electrodes. The baseline algorithm monitoring sub-process 2003 is then repeated.

Please replace previous paragraph 107 (now paragraph 112 with the insertion) with the following paragraph:

[107] Step 2041 determines whether to adapt the detection algorithm. If the detection algorithm is not adapted, step 2048, as describer later, is next executed. If ~~so~~ the detection algorithm is adapted, step 2043 enables the physician to provide a training set (e.g., cluster data for previous seizures) so that the detection algorithm may enhance performance by adjusting its parameters. The use of filter adaptation for detecting seizures is disclosed in U.S. Patent No. 5,995,868 entitled "System for the Prediction, Rapid Detection, Warning, Prevention, or Control of Changes in Activity States in the Brain of a Subject" and is incorporated herein in its entirety. In sub-step 2043, the physician identifies collected neurological data that characterizes the seizure (e.g., one or more detection clusters that are associated with the seizure). The detection algorithm may be adapted using different methods, as requested by the physician or automatically (unsupervised learning). With one variation of the embodiment, the detection algorithm, in step ~~2044~~ 2045, is adapted by adjusting threshold and time duration settings in order to approximately optimize seizure detection in relation to the data identified in sub-step 2043. In step ~~2045~~ 2047, the physician evaluates the adaptation results. In step ~~2046~~ 2047, if the adaptation is satisfactory, the physician may accept recommended settings through an input device in step 2047. However, if the adaptation is not satisfactory, as determined ~~by~~ in step ~~2046~~, 2047, the physician may reject the recommended settings. In step 2048 ~~is executed to determine~~, it is determined whether to record more seizures. If ~~so~~ more seizures need to be recorded, baseline algorithm monitoring sub-process ~~2003~~ 2005 continues to execute for subsequent seizures. Otherwise, process 2000 proceeds to trial screening sub-process 2151.

Please replace previous paragraph 111 (now paragraph 116 with the insertion) with the following paragraph:

[111] If the therapy is not deemed successful in step 2168, algorithm adaptation may be performed in step 2170. Step 2170 essentially functions as in step 2041. If step 2170 determines that algorithm adaptation shall not be performed, step 2171 is next executed. Otherwise, step 2172 determines whether algorithm parameters shall be changed. If so, step 2167 is executed;

otherwise, step 2171 is executed. In step 2171, the electrodes may be reconfigured and step 2153 may be repeated. In a variation of the embodiment, restimulation of electrodes may be expanded to electrodes that are involved in the seizure other than the first or second electrode as determined in sub-step 2021. If subsequent trial screening shall not try different electrodes or stimulation settings (as determined by the physician), sub-process 2151 is completed and the electrodes may be explanted. If the therapy is deemed successful in step 2168, sub-process 2151 is completed and the trial ends in step 2173 and the leads are internalized and the IPG implanted in step 2175.

Please replace previous paragraph 117 (now paragraph 122 with the insertion) with the following paragraph:

[117] Before a user-defined treatment therapy configuration is even tested or stored, the medical device system preferably performs a charge density check. For example, in the embodiment of electrical stimulation therapy, the medical device system computes the charge density of the stimulation configuration using the impedance of the electrode configuration, voltage level, stimulation pulse width and contact geometry of the electrode configuration. The charge density may be computed using the following formula:

$$(I \cdot \Delta w)/(\text{surface area of electrode})$$

where I is the current of the stimulation pulse and is approximately equal to the voltage level divided by the impedance, and Δw is the pulse width. If the calculated charge density exceeds a preset threshold, the medical device system considers the stimulation configuration to be not valid and prevents and/or warns the user from testing with the associated stimulation configuration. In a preferred embodiment, the preset threshold is approximately 30 μcoulombs/cm^2/phase and can be in the range of up to 500 μcoulombs/cm^2/phase. The preset threshold can be programmable and, of course, may vary depending on the nervous system disorder being treated and/or the medical device system. For example, co-pending U.S. Patent Application No. 10/099,436, Goetz et al., "Automated Impedance Measurement of an Implantable Medical Device," and filed on March 15, 2002 (now U.S. Patent No. 6,978,171)

discloses apparatus and method for automating impedance measurements of sets of electrodes that are associated with a lead of an implanted device. Alternatively, in another embodiment, the current may be measured directly for each electrode and the value may be used to compute the charge density.

Please replace previous paragraph 175 (now paragraph 180 with the insertion) with the following paragraph:

[175] Steps 2701 through 2731 ~~2701-2731~~, as shown in Figure 27, may be sequentially executed. However, in a variation of the embodiment some of the steps may be executed in parallel while other steps may be sequentially executed. For example, step 2701 (start/continue signal processing) may be executed in parallel with step 2731 (data storage).